

Concurrent salmonellosis and histoplasmosis in AIDS: an unusual co-existence in Britain

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Abstract

A patient is described with systemic salmonellosis which was unresponsive to therapy. *Histoplasma capsulatum* was isolated after death and we suggest that dysfunction of the reticuloendothelial system by *H. capsulatum* may have altered the prognosis.

Introduction

Both disseminated *Histoplasma capsulatum* and non-typhi salmonella bacteraemia are manifestations of immunosuppression in patients infected with human immunodeficiency virus (HIV) and are AIDS-defining diagnoses. In the non-immunocompromised salmonella bacteraemia occurs in 5% of patients with infection, but rates of 40% to 80% are reported in the immunocompromised^{1,2} and invasive infection requires prompt antibiotic therapy. Post-treatment relapse in the immunocompromised remains a problem and long-term suppressive therapy is indicated.^{3,4}

Histoplasmosis was initially reported in patients with AIDS in 1982 though it had previously been recognised as an opportunistic pathogen in those with defective cellular immunity. Nearly all cases associated with AIDS are disseminated, and it is often the first opportunist infection in endemic areas. In one report from Houston histoplasmosis was the first opportunist infection in 75% of cases of AIDS.⁵ In the UK, however, histoplasmosis in AIDS is attributed to reactivation of disease contracted in endemic areas and is therefore infrequent.

Involvement of the reticuloendothelial system with macrophages full of yeast cells is a pathological hallmark in histoplasmosis. It has been suggested that, as a result of macrophage dysfunction, an impaired ability to kill intracellular pathogens such as salmonella may occur.⁶ Dual infection with *Histoplasma* and salmonella has been reported in only two patients with AIDS previously, both of whom were from the U.S.⁶

Case report

A 26 year old HIV-antibody positive homosexual Brazilian man presented with a 3 month history of diarrhoea, intermittent fever, and weight loss. Two weeks prior to admission he noted a facial skin rash, dry cough and dyspnoea. He had been an infrequent attender to outpatients and had declined zidovudine therapy. His T cell subset count 8 months prior to admission was 194/mm³. He had not recently travelled to South America.

On examination he was pyrexial (38.6°C), cachexic, and anaemic. He had generalised lymphadenopathy, pustular facial rash, and oral candidosis.

Initial investigations revealed: Hb 8.8 g/dl, WBC $2.0 \times 10^9/l$, total lymphocyte count $0.2 \times 10^9/l$, platelet 130×10^9 ; Chest radiograph was normal; liver function tests were normal, except albumin 15 g/l; mid-stream urine culture sterile; stool cultures negative; blood cultures grew *S. typhimurium* after 36 hours.

Treatment was commenced with ciprofloxacin (200 mg b.d. intravenously for 24 hours and subsequently 750 mg b.d. orally). He remained unwell and pyrexial, and continued to deteriorate. Blood cultures were sterile after 4 days and remained so until death.

Histoplasma antigen complement fixation test and immunodiffusion tests were negative. A skin biopsy performed shortly before death grew *H. capsulatum* on culture, the result not being known until after death; histological examination was unhelpful.

He died 18 days after admission. Post mortem examination confirmed the presence of yeast-like organisms consistent with *H. capsulatum* in macrophages in the tongue, testes, skin, spleen, lymphnodes and the reticuloendothelial cells of the liver.

Discussion

The clinical features of disseminated histoplasmosis are nonspecific, most patients presenting with symptoms of fever and weight loss. The infection usually begins in the lungs, probably as a result of reactivation, though pulmonary features may not be present, and the chest radiograph may be normal as in this case. When untreated severe clinical manifestations resembling septicaemia may ensue, and as patients are often concurrently infected with other opportunist pathogens a careful diagnostic search is required. Cutaneous manifestations, including pustular, follicular, maculopapular, and erythematous lesions, occur in up to 17% of cases.⁷

Since the prognosis is better if treatment is begun early it is important to establish the diagnosis rapidly. Isolation of *H. capsulatum* in cultures from a variety of body tissues proves the diagnosis in most cases, and histopathologic staining of tissue sections or peripheral blood smears with Gomori methenamine silver provides a means for rapid diagnosis. Anti-*H. capsulatum* antibody detection by immunodiffusion or complement fixation also has a role with sensitivity approaching 7%.⁷

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The coexistence of disseminated histoplasmosis in association with salmonellosis in this case, may, as a result of impaired macrophage function, have prevented antibacterial therapy from being effective. Wheat *et al*⁶ suggested that reticuloendothelial "blockade" may result from this intracellular yeast. "Blockade" of the reticuloendothelial system is characteristic of sickle cell anaemia, bartonellosis, and louse-borne relapsing fever and serious *Salmonella* infection occurs in these diseases.

Ampicillin, chloramphenicol and co-trimoxazole are effective in invasive non-typhi salmonellosis, but the lack of bactericidal activity against *Salmonella spp* at clinically achievable levels, and the toxicity of chloramphenicol and co-trimazole, particularly in those infected with HIV, constrain their use.⁸ The quinolones are active against salmonella, with excellent intracellular penetration and concentrations within neutrophils and macrophages.⁹ Ciprofloxacin has been used with success in immunocompromised patients¹⁰ and hence its choice in the case described.

This case highlights the need for clinicians to maintain their awareness of the possible coexistence and interaction of pathogens in AIDS patients. When salmonellosis is diagnosed and there is a poor response to treatment disseminated histoplasmosis should also be con-

sidered. Treatment with amphotericin B is highly effective in histoplasmosis and may, in this case, have altered the outcome.

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